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EXAMINER	
FOX, DAVID T	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,430	WERNER ET AL.	
	Examiner	Art Unit	
	David T. Fox	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *14-17,21-29,35 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-20,30-34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/2/05 & 4/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Restriction/Election

Applicant's election with traverse of Group I in the reply filed on 30 April 2008 is acknowledged. The traversal is on the ground(s) that the prior art cited by the Examiner does not teach all of the features of the instant invention, namely the destruction of seeds once the product has been isolated, the minimization of gene silencing, the production of large quantities of product in the seed, and the use of sterile seed. This is not found persuasive because seed destruction or seed sterility is not claimed in the instantly elected invention. Regarding gene silencing, it appears that this would be an inherent property of the progeny taught by the prior art, since the prior art process utilizes the same isolation of genes in individual parents as instantly claimed. Regarding the production of the product in the seed, the prior art utilizes a constitutive promoter which would result in the production of product in the seed. Furthermore, the utilization of the seed as an organ of high gene expression and easy storage is well-known in the art, as stated below.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-37 are pending. Claims 14-17, 21-29, 35 and 37 are withdrawn. Claims 1-13, 18-20, 30-34 and 36 are examined in the instant Office action.

Claims 5-8 and 18-19 are objected to for reading on a non-elected invention, namely replicating RNA.

Foreign Priority

The foreign priority document filed 06 June 2003 has been reviewed, and is deemed to provide full support for the instantly claimed invention.

Specification Objections

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant's submission of the first page of the published international application, which includes an Abstract, is noted. However, that page also includes extraneous material besides the Abstract, which cannot be deleted from the Image File Wrapper.

The specification is further objected to for not reciting the continuity data. Page 1 of the specification should be amended to insert the following paragraph under the title:

---CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 371 of PCT/EP04/06069 filed 04 June 2004.---

Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 20, 33 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in its recitation of "chemical compound like a polymer" which fails to positively recite a required claim element. It is unclear whether polymers or polymer-like compounds are being claimed, or whether the recitation of "polymer" is merely exemplary of the class of compounds being claimed.

Claim 20 is indefinite in its recitation of "based on a geminivirus" as the degree of derivation is unclear. It is unclear how much geminivirus genetic material would be retained by a replicating nucleic acid that is somehow "based on" a geminivirus.

Claim 33 is indefinite in its recitation of "preferably being a protein" which fails to positively recite a required claim element. It is unclear whether a protein is merely exemplary or required.

Claim 36 is indefinite in its recitation of "produced or producible" which appears to be redundant.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-13 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any "replicating DNA" from any source and of any sequence, comprising a multitude of undefined genes or subsequences therein. Replicating DNAs from a multitude of DNA viruses (and not limited to plant viruses) are contemplated in the specification, as are autonomously replicating DNA plasmids from a multitude of non-viral sources. See, e.g., page 7 of the specification, second paragraph,

where it is stated that the replicating DNA or RNA "*may be* of plant viral origin" [emphasis added]. See also page 7 of the specification, top paragraph, where the general category of viruses (presumably including animal viruses) are contemplated as sources of the replicating DNA. See also page 17 of the specification, bottom paragraph, where plant DNA is contemplated as the source of autonomously replicating plasmids.

In contrast, the specification only provides guidance for replicating DNA comprising a plant geminivirus origin of replication and a plant geminivirus replicase gene. No guidance has been provided for replicating DNA from any other type of DNA virus, from any non-viral organism, from any non-plant virus, or from other geminiviral genes or sequences. Furthermore, no guidance has been provided for the conservation of particular sequences throughout the broadly claimed genus which are associated with the function of replicating in plants.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed

genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP, Eighth Edition, Section 2163, page 174 of Chapter 2100 of the September 2007 revision, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description

Requirement Guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Enablement

Claims 1-3, 5-13, 18-20, 30-34 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for utilizing a replicating DNA comprising a plant geminiviral origin of replication and a plant geminiviral replicase gene, wherein the replicating DNA further comprises a divisible gene encoding a protein of interest, and wherein a functional protein product is isolated from transformed seeds comprising the rejoined portions of the protein-encoding gene; does not reasonably provide enablement for claims broadly drawn to the use of any non-exemplified replicating DNA from a multitude of non-exemplified sources, or for the production and isolation of non-exemplified functional products such as RNA or polymers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 5-13 and 18-20 are broadly drawn to any "replicating DNA" from any source and of any sequence, comprising a multitude of undefined genes or subsequences thereon. Replicating DNAs from a multitude of DNA viruses (and not limited to plant viruses) are contemplated in the specification, as are autonomously replicating DNA plasmids from a multitude of non-viral sources. See, e.g., pages 7 and 17 of the specification as discussed above.

In contrast, the specification only provides guidance for replicating DNA comprising a plant geminivirus origin of replication and a plant geminivirus replicase gene. No guidance has been provided for replicating DNA from any other type of DNA virus, from any non-viral organism, from any non-plant virus, or from other geminiviral genes or sequences. Furthermore, no guidance has been provided for the replication of DNA in transformed plants, or for the maintenance in said replicating DNA of foreign DNA encoding desired products, following the introduction of said non-exemplified replicating DNA.

Claims 1-3, 5-13, 18-20, 30-34 and 36 are broadly drawn to the use of sequences encoding a multitude of "products of interest" including proteins, RNA, or chemical compounds including polymers; wherein said sequences may be split and transferred to individual parent plants each containing a portion of the "genetic endowment" encoding said products, wherein said products are produced by the combination of different "genetic endowments" in F1 seed; and wherein said products may be isolated from seeds and are functional.

In contrast, the specification only provides guidance for the isolation of protein-encoding genes which may be divided into subsequently recombinable "genetic endowments", and for the isolation of functional proteins from F1 seeds in which "partial genetic endowments" have been recombined. No guidance is provided for the identification of a multitude of non-exemplified genes encoding a multitude of non-exemplified RNA or polymer products, wherein said genes may be split and later recombined for the production of intact, functional products. Moreover, no guidance has

been provided for the isolation of non-protein products such as RNA from seeds, or for the use of said RNA products.

The use of replicating nucleic acid from viruses for the introduction and maintenance of foreign genetic material in plants is unpredictable. Dawson et al teach that the introduction into plant cells of a replicating nucleic acid comprising the insertion of an exogenous CAT gene into a tobacco mosaic virus-derived RNA molecule encoding a tobacco mosaic virus (TMV) coat protein, under the control of a TMV subgenomic promoter, resulted in deletion of the exogenous sequence and/or lack of replication in plant cells in which the replicating nucleic acid molecules had been introduced (see, e.g., page 285, Abstract; and pages 289-291). Such deletion or lack of replication would not result in the production of a product of interest.

Hohn et al teach that non-geminiviral DNA viruses such as cauliflower mosaic virus (CaMV), when used as viral vectors to introduce replicating DNA which encodes a desired product, are limited by rearrangements or deletion of the product-encoding sequences (see, e.g., paragraph bridging pages 188 and 189). Such deletion or rearrangement would not result in the production of a functional product of interest.

Moreover, the production in transformed plant cells of functional non-exemplified products, such as RNA or chemical compounds whose synthesis depends upon enzymes encoded by the introduced nucleic acid, is unpredictable. Colliver et al teach that transformation of bird's foot trefoil with a construct encoding antisense RNA to bean chalcone synthase unexpectedly resulted in transformants with *increased* levels of the

chalcone synthase transcripts (see, e.g., page 519, left column, second paragraph). Thus, the RNA product did not have the desired function of inhibiting gene expression.

Stephanopoulos et al teach that plant transformation with an enzyme involved in the synthesis of a desired product may be hampered by feedback inhibition, compensation from other enzymes involved in the metabolic pathway, or failure to identify the rate-limiting step of the pathway (see, e.g., page 392, Abstract; page 393, column 2, penultimate paragraph; page 394, column 2, penultimate paragraph; paragraph bridging pages 394 and 395.)

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to isolate a multitude of non-exemplified replicating sequences from a multitude of non-exemplified sources including non-viruses, animal viruses, non-geminiviral DNA viruses, or geminiviral sequences other than the origin of replication and the replicase gene; and to evaluate these sequences for their ability to effect DNA replication and maintenance of the desired transgene in plant cells and plants transformed therewith. Undue experimentation would have also been required by one skilled in the art to identify and evaluate a multitude of divisible genes encoding a multitude of functional non-exemplified RNA or polymer products, following the putative recombination of the divisible genes in an F1 seed.

Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 31, 34 and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Szarka et al (US 7,098,383 filed 21 June 2002).

Claims 1-4, 31 and 34 are drawn to a process for producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent, each parent comprising a "partial genetic endowment" which by itself is insufficient to encode the desired product in the individual parents; wherein the combination of said partial genetic endowments in the F1 hybrid seed results in the generation of a complete genetic endowment encoding the protein of interest; wherein said protein of interest is isolated from the F1 seed; and wherein the transformed plants may be monocots or dicots. Claim 36 is drawn to an F1 hybrid seed produced by this process.

Szarka et al teach the transformation of dicotyledonous Arabidopsis plants with partial genetic endowments encoding either the light or heavy chain of a multimeric immunoglobulin antibody protein, wherein said partial genetic endowments comprise a seed-specific promoter for the production of the protein in the seed, wherein the hybridization of parent plants containing either the light- or heavy- chain encoding partial genetic endowments results in the production in F1 hybrid seeds of the multimeric immunoglobulin antibody which is the product of interest; wherein the proteinaceous

antibodies are produced as cleavable fusion proteins linked to an oil body protein (or "oleosin"), wherein the oil bodies comprising said fusion proteins may be easily isolated from the seeds via centrifugation, and wherein the desired protein product of interest may be easily isolated from the oil body by enzymatic cleavage (see, e.g., column 1, lines 26-32; column 2, lines 5-40; column 3, line 38 through column 4, line 58; column 6, lines 3-53; column 10, lines 5-7; column 11, line 55 through column 12, line 4; column 16, line 55 through column 17, line 28; column 17, line 54 through column 18, line 16; column 19, Table 1; column 20, lines 44-58; column 36, lines 33-58; column 48, lines 48-56; column 56, line 41 through column 57; column 63, line 55 through column 64, line 38; column 65, lines 8-23; and claims 33-43).

Claim 30 is rejected under 35 U.S.C. 102(e) as being anticipated by Szarka et al (US 7,098,383 filed 21 June 2002) as evidenced by Sengupta-Gopalan et al.

Claim 30 is drawn to the process above wherein the product of interest accumulates in the embryo.

Szarka et al teach the production of a multimeric proteinaceous immunoglobulin product, wherein the genes encoding the single chain portions of the product were operably linked to the seed-specific phaseolin promoter, as discussed above (see, e.g., column 10, lines 5-7; column 36, lines 23-58; column 65, lines 8-23). The phaseolin promoter inherently directs gene expression selectively in the embryo of the seed (see, e.g., Sengupta-Gopalan et al, page 3320, Abstract).

Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by each of Yadav (6,077,992) and EP 1,048,734 (SCRIPPS RESEARCH INSTITUTE).

Claim 36 is drawn to a seed comprising both "partial genetic complements" which when combined are sufficient for the production of a desired product of interest; wherein the seed is "produced or producible" from a process comprising hybridizing parent plants each containing a single "partial genetic complement", followed by isolation of the desired product from the seed.

Each of Yadav and SCRIPPS RESEARCH INSTITUTE (hereinafter "SCRIPPS") teach an F1 hybrid seed comprising recombined partial genetic complements sufficient for the production of a proteinaceous product of interest, wherein the seed was produced by hybridizing parent plants each containing a single "partial genetic complement", as discussed below.

Yadav teaches a process for producing soybean and corn seeds which comprise a replicating DNA comprising a geminiviral origin of replication and a geminiviral replicase and further comprising a gene encoding a desired proteinaceous product of interest, wherein said seeds were produced by hybridizing parent plants containing only one of these elements, wherein the simultaneous occurrence of both of these elements results in the production of an autonomously replicating geminiviral DNA for high levels of production of a product of interest in the seed, wherein seed-specific promoters including the phaseolin promoter are utilized for high levels of product in the seed (see, e.g., Figure 1; column 1, lines 17-20; column 1, line 57 through column 2, line 39; column 2, lines 58-67; column 4, line 58 through column 5, line 34; column 5, lines 59-65; column 6, lines 12-18; column 10, line 23 through column 11, line 31; column 12, lines 22-43; column 12, line 59 through column 13, line 3; column 13, line 19 through

column 14, line 49; column 16, line 56 through column 17, line 20; column 17, lines 58-67; column 18, lines 30-67; column 19, line 33 through column 22, line 51; claims 15-22).

SCRIPPS teaches a process for producing F1 tobacco seeds and plants comprising crossing parent plants each containing a partial genetic endowment comprising a sequence encoding a light or heavy chain of a multimeric antibody, wherein the proteinaceous product of interest comprising a multimeric antibody is produced in said F1 plants, said sequences operably linked to the constitutive CaMV 35S promoter which causes expression in all plant tissues including the seed, and wherein the protein is isolated from the F1 plant tissue (see, e.g., page 3, lines 3-20 and 40-47; page 4, lines 3-10; page 5, lines 36-39; page 12, lines 19-29; page 26, lines 38-53; page 27, lines 34-49; page 28, lines 8-13 and 26-40; page 29; Figures 1-3 and 5).

If claim 36 is interpreted as being drawn to seeds "producible" by the process of claim 1, then each of Yadav or SCRIPPS teach seeds comprising the same genetic endowment as the seeds produced by the method of claim 1. Thus, each of Yadav or SCRIPPS teach seed which may be "producible" by the process of claim 1, but which also may be "producible" by an alternate process, including the processes taught by each of the prior art references, which do not explicitly teach the final step of claim 1 comprising protein isolation from the seed.

Neither Yadav nor SCRIPPS teach the actual isolation of the protein of interest from the seed, as ultimately claimed in claim 1 upon which claim 36 depends, if claim 36 is interpreted as being drawn to seed "produced" from the process of claim 1. However,

they do teach the same process for producing the seed prior to said isolation, as stated above. The failure to teach the final step of the claimed process for making the seed, said step comprising the isolation of protein from the seed, would not impart a unique characteristic to the seed itself, which would distinguish the prior art seed from the instantly claimed seed.

See *In re Best*, 195 USPQ 430, 433 (CCPA 1977), which teaches that where the prior art product seems to be identical to the claimed product, except that the prior art is silent as to a particularly claimed characteristic or property, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention.

See *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985), which teaches that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process, if the process of making the product fails to distinguish the two products.

Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 30-31, 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1,048,734 (SCRIPPS) in view of Fiedler et al.

Claims 1-4, 30-31 and 34 are drawn to a process for producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent, each parent comprising a "partial genetic endowment" which by itself is insufficient to encode the desired product in the individual parents; wherein the combination of said partial genetic endowments in the F1 hybrid seed results in the generation of a complete genetic endowment encoding the protein of interest; wherein said protein of interest is produced in seed tissues including embryo, endosperm, or cotyledons, and wherein said protein of interest is isolated from the F1 seed; and wherein the transformed plants may be monocots or dicots. Claim 36 is drawn to an F1 hybrid seed produced by this process.

SCRIPPS teaches a process for producing a multimeric immunoglobulin protein of interest in dicotyledonous tobacco F1 plants and seeds, said multimeric protein comprising a heavy and a light chain each encoded by a partial genetic endowment in each parent of the F1 seed, said chain-encoding endowments operably linked to a

constitutive promoter, and wherein the multimeric immunoglobulin protein of interest is isolated from plant tissue derived from the F1 seed, as stated above.

SCRIPPS does not teach the actual isolation of the multimeric protein of interest from the F1 seed itself.

Fiedler et al teach the advantages of the seed for high levels of expression of proteins of interest, wherein the seed is also a vehicle for long-term storage of the functional protein of interest, wherein the protein of interest includes an immunoglobulin protein, wherein the immunoglobulin-encoding sequence is operably linked to a seed-specific legumin promoter, and wherein the protein was isolated from the transformed F1 hybrid seed (see, e.g., page 1090, column 1, top two paragraphs and column 2, second full paragraph; paragraph bridging pages 1090 and 1091; page 1091; page 1092, Figure 3 and column 2, second paragraph). The seed-specific promoter would inherently cause expression in at least one of the seed tissues recited in claim 30.

It would have been obvious to one of ordinary skill in the art to utilize the method of hybridizing parental plants for the production of a multimeric immunoglobulin protein of interest in F1 seeds as taught by SCRIPPS, and to modify that method by incorporating the seed-specific promoter and actual product isolation from seed as taught by Fiedler et al; given the teachings of Fiedler et al of the advantages of seed-specific expression and ultimate product isolation therefrom. The substitution of a known seed-specific promoter for a known constitutive promoter would have been the obvious substitution of equivalents in the same art area, which would have been expected to predictably function in their known and expected manner.

Claims 1, 3-9, 13, 18-20, 30-31, 33-34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yadav (US 6,077,992).

Claims 5-9, 13, and 18-20 are drawn to a process of producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent, each parent comprising a "partial genetic endowment"; wherein the combination of said partial genetic endowments in the F1 hybrid seed results in the generation of a complete genetic endowment encoding the protein of interest; wherein said protein of interest is isolated from the F1 seed; and wherein the combination of the partial genetic endowments in the F1 seed results in a replicating DNA which encodes said protein of interest, wherein the replicating DNA may be derived from a plant geminvirus or be an autonomous plasmid, and wherein constitutive or seed-specific promoters may be involved. Claim 33 is drawn to the above method wherein the female parent of the F1 hybrid seed provides the coding sequence for the protein of interest.

Yadav teaches a process for producing dicotyledonous soybean and monocotyledonous corn seeds which comprise a replicating DNA comprising a geminiviral origin of replication and a geminiviral replicase and further comprising a gene encoding a desired proteinaceous product of interest, wherein said seeds were produced by hybridizing parent plants containing only one of these elements, wherein the simultaneous occurrence of both of these elements results in the production of an autonomously replicating DNA for high levels of production of a product of interest in the seed, wherein seed-specific promoters including the phaseolin promoter are utilized for high levels of product in the seed, as discussed above. Yadav teaches the advantages

of producing the product of interest in seed tissue (see, e.g., column 12, lines 22-32; column 14, lines 35-48; column 22, lines 29-44).

Yadav does not teach the actual isolation of the product of interest from the seed.

It would have been obvious to one of ordinary skill in the art to utilize the method for producing high levels of proteins or other products of interest in F1 hybrid seeds as taught by Yadav, and to modify that method by actually isolating the desired product from the seed, as the ultimate goal of the method taught by Yadav, using known protein isolation techniques, for predictable results. It would have been further obvious to utilize the parent which comprises the protein of interest-encoding sequence as the female parent, given the knowledge by those of ordinary skill in the art that seeds are produced by the female parent, in the absence of unexpected results.

Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yadav (US 6,077,992) as applied to claims 1, 3-9, 13, 18-20, 30-31, 33-34 and 36 above, and further in view of Lyznik et al (US 7,164,056 filed 03 May 2002).

Claims 10-12 are drawn to a method for generating a replicating DNA in F1 hybrid seed for the production of high levels of a product of interest including a protein of interest, wherein the replicating DNA is generated by the action of site-specific recombination and a recombinase-encoding gene.

Yadav teaches a method for generating a replicating DNA in F1 hybrid seed for the production of high levels of a product of interest including a protein of interest, as stated above, wherein the replicating DNA comprises a geminiviral origin of replication and is generated by the action of the geminiviral replicase, as facilitated by tandem

repeats of geminiviral sequences including the origin of replication (see, e.g., Figure 1; column 5, lines 47-48; column 10, lines 43-67).

Yadav does not teach the use of a recombinase system for the generation of the replicating DNA.

Lyznik et al teach a geminiviral system comprising a proreplicon which comprises a "target sequence" including a protein-encoding sequence, said "target sequence" to be introduced into the genome of a recipient monocot or dicot plant; wherein the proreplicon comprises a geminiviral origin of replication and a geminiviral replicase gene; wherein parent plants comprising one of the above components may be crossed to generate said replicating geminiviral DNA encoding the proteinaceous product of interest in F1 hybrid seeds, wherein the protein of interest may be isolated from the plant tissue by known means; wherein seed-specific promoters may be used; and wherein a recombinase gene and recombination sequences may be used to generate the replicating DNA (see, e.g., column 1, lines 43-56; column 4, lines 29-36 and 52-57; column 5, lines 4-19; column 8, lines 7-28; column 15, lines 20-26 and 38-47; column 16, lines 1-14; column 19, lines 28-47; column 23, lines 19-33; column 27, line 53 through column 28; column 29, line 46 through column 30, line 3; column 32, lines 21-47; column 32, line 53 through column 33, line 34; column 34, lines 23-29; column 38 through column 39, line 2; claims 8-10 and 15-18).

It would have been obvious to one of ordinary skill in the art to utilize the geminivirus-mediated method of generating replicating DNA encoding a product of interest in F1 hybrid seeds, as taught by Yadav: and to modify that method by

incorporating the recombinase/recombination sequences for the generation of geminiviral replicating DNA encoding a proteinaceous product of interest, as taught by Lyznik et al. The substitution of one known replicating DNA-generating means for another known equivalent in the same art area, namely a recombination system, would have been expected by one of ordinary skill in the art to predictably function in the same way.

Claims 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szarka et al as applied to claims 1-4, 30-31, 34 and 36 above, and further in view of WO 98/37211 (GENE SHEARS).

Claims 32-33 are drawn to a process for producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent, each parent comprising a "partial genetic endowment" which by itself is insufficient to encode the desired product in the individual parents; wherein the combination of said partial genetic endowments in the F1 hybrid seed results in the generation of a complete genetic endowment encoding the protein of interest; wherein said protein of interest is isolated from the F1 seed; and wherein the female parent of the F1 hybrid is male sterile and/or comprises the protein of interest-encoding gene.

Szarka et al teach a process for producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent, each parent comprising a "partial genetic endowment" which by itself is insufficient to encode the desired product in the individual parents; wherein the combination of said partial genetic endowments in the F1 hybrid seed results in the generation of a complete genetic endowment encoding

the protein of interest; wherein said protein of interest is isolated from the F1 seed, as discussed above.

Szarka et al do not teach the use of a female parent of the F1 hybrid which is male sterile or which comprises the protein of interest-encoding gene.

GENE SHEARS teaches a method for producing a protein of interest comprising crossing two plants, wherein the protein of interest may confer male sterility which is advantageous for pollination control during hybrid production, or wherein the protein of interest may be an enzyme (including a multimeric enzyme) involved in the production of a useful compound in plants, and wherein a female parent comprising the protein-encoding gene under the control of a regulatable promoter may be utilized for increased control of gene expression, and wherein seed-specific promoters may be utilized (see, e.g., page 1, lines 3-5; page 8, lines 15-19; page 9, line 30 through page 10, line 6; page 11, lines 1-20; page 12, lines 1-26; page 13, line 10 through page 14, line 14; page 15, lines 17-28; page 21, line 24 through page 22, line 2; page 28, lines 1-21; pages 36-37).

It would have been obvious to one of ordinary skill in the art to utilize the method of producing a protein of interest in an F1 seed obtained by hybridizing a first and second transgenic parent as taught by Szarka et al, and to modify that method by incorporating male female sterile plants and/or female plants which comprise the genetic component necessary for the production of the protein of interest as taught by GENE SHEARS. The incorporation of a known technique into a process of the same art area would have been obvious to one of ordinary skill in the art, who would have

expected each to predictably function in its known and expected manner. The use of male sterility for controlled pollination in hybrid seed production is well known in the art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (571) 272-0795. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/David T Fox/

Primary Examiner, Art Unit 1638

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